

## Cancer and non-cancer epidemiological study in the high background radiation area of Yangjiang, China

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**Abstract.** The major objective of this study is to examine cancer mortality risk associated with low-level radiation exposure occurring in the high background radiation area (HBRA) in Yangjiang of Guangdong Province, China. The average annual effective doses received by the inhabitants from natural sources of external and internal exposures in HBRA are estimated to be 2.10 and 4.27 mSv, respectively, and the corresponding doses in the control area (CA) to be 0.77 and 1.65 mSv. We analyzed the mortality of non-cancer diseases as well in order to shed light on the comparability of the HBRA and the CA. We examined mortality for cancer and non-cancer diseases during the period 1979–1998. The prospective mortality study followed 125,079 subjects during the period 1979–1998, accumulated 1,992,940 person-years (PYs) at risk, and ascertained 12,444 deaths, including 1202 cancer deaths. The mortality of all cancer showed no difference between the HBRA and the CA [relative risk (RR)=1.00; 95% confidence interval (CI), 0.89 to 1.14]. When cancer deaths were limited to persons with pathological diagnosis, the RR changed only slightly (RR=0.99; 95% CI, 0.78 to 1.26). The RR was not evidently modified by sex or age or follow-up period (1979–1986, 1987–1998). In site-specific cancer mortality analysis, only cancer of the esophagus showed a statistically significant excess in the HBRA (RR=2.61; 95% CI, 1.11 to 7.66). However, the observed excess mortality of esophageal cancer did not show a monotonic increase with external radiation dose or cumulative lifetime dose. The RR comparing non-cancer mortality in the HBRA with that in the CA was 1.06 (95% CI, 1.01 to 1.10), which was a statistically significant increase. However, the excess was limited to those aged under 50 and the latter half of the observation period (the period 1987–1998), suggesting that the excess mortality may be due to recent changes in lifestyles of the

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younger generations. In the cause-specific analysis of non-cancer deaths, disease of the digestive organs showed a statistically significant increase. This appears to be mainly due to liver diseases. In conclusion, the present study showed no increase of cancer mortality in the HBRA. However, it is difficult for the present study to support or deny the possibility that the radiation-related cancer risk associated with chronic exposure to low-dose radiation may be different from the risk associated with high dose ranges or high dose-rate exposure. The observed increase of non-cancer mortality in the present study is unlikely to be attributable to radiation exposure. © 2004 Published by Elsevier B.V.

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## 1. Introduction

An epidemiological study in the high background radiation area (HBRA) of Yangjiang in Guangdong province, China, has been carried out since 1972. The primary objective of this study is to examine the cancer mortality risk associated with naturally occurring high background radiation exposure by comparing mortality rates here to those in the neighbouring control area (CA). In addition, the mortality of non-cancer diseases is compared between the HBRA and the CA in order to shed further light on the comparability of the two areas. The average annual effective doses received by the inhabitants from natural sources of external and internal exposures in the HBRA were estimated to be 2.10 and 4.27 mSv, respectively, and the corresponding doses in the CA to be 0.77 and 1.65 mSv.

In 2000, we reported the results of a cancer mortality study covering the period 1979–1995 [1]. In this paper, we present the results from the analysis of combined data for the periods from 1979 to 1986, and from 1987 to 1998, adding 3 years to our previous report.

## 2. Materials and methods

The mortality data for the period 1979–1986 were collected by a prospective follow-up survey of dynamic populations, consisting of around 80,000 inhabitants in the HBRA and as many in the CA. The mortality data for 1987–1998 were obtained from a prospective follow-up survey of a fixed cohort consisting of 106,517 individuals alive as of the January 1, 1987. The methods of mortality follow-up survey are described in detail elsewhere [2]. In brief, trained local census takers surveyed the hamlets of the study areas to collect information on deaths and migrations among the inhabitants in each hamlet. The collected information was recorded in the demographic survey sheet prepared for each household in the hamlet. The members of task group on cancer mortality then visited the studied areas and reviewed the survey sheets. In order to ascertain the cause of death, they visited all the major hospitals in the study area, and reviewed medical records of the deceased and extracted relevant information. If necessary, they revisited the local village doctors and the family members or next of kin to collect further information on cause of death. The underlying cause of death thus was ascertained and coded according to the 9th revision of the International Classification of Diseases (ICD-9).

The cumulative individual dose to each cohort member was estimated on the basis of measurements of external exposure to natural radiation source. The external doses were

estimated by environmental dose rate measured with scintillation survey-meters and converted into the annual absorbed doses considering the occupancy factors specific for both sex and age. For the internal doses, 4.27mSv for the HBRA and 1.65 mSv for the CA, two fixed annual values, were used in estimating the individual lifetime cumulative dose. Based on the hamlet-specific average external dose rates, the cohort members were categorized into four dose groups for internal comparison: the high, intermediate, and low dose-rate groups in the HBRA, and the control group in the CA. The average annual effective (external) doses ( $10^{-5}$  Sv/a) for each group were 246.07 (224.10–308.04), 210.19 (198.07–224.09), 183.31 (125.29–198.06, and 67.92 (50.43–95.67), respectively [3].

The estimates of relative risk (RR) and excess relative risk coefficients (ERRs per Sievert) and their 95% confidence interval (CI) were obtained from Poisson regression analysis using the AMFIT in Epicure.

### 3. Results

Through 1979 to 1998, 1,992,940 person-years (PYs) at risk were accumulated with the follow-up of 125,079 subjects, 12,444 deaths including 1202 cancer deaths, 1204 deaths from external causes (injury and poisoning), and 10,038 cases from non-cancer disease except external causes were identified.

#### 3.1. Cancer mortality

Cancer deaths yielded a total of 1202 cases, making up 9.7% of all causes of death. The first-five leading cancer sites, accounting for 68.5% of all cancer deaths, were cancers of the liver, nasopharynx, lung, and stomach, and leukaemia.

The sex- and age-adjusted RRs (95% CI) for certain special types of cancers by dose group are presented in Table 1. The RR for overall cancers was 1.00 (95% CI, 0.89 to 1.14), indicating that there was no difference in overall cancer mortality between the HBRA and the CA. The RRs for site-specific cancers of the nasopharynx, stomach, colon, liver, lung, bone, and female breast were at a level of less than one; the RRs for cancers of the esophagus, rectum, pancreas, skin, cervix uterus, thyroid, brain, and central nervous system, as well as those for leukaemia and lymphoma, were larger than one. However, only cancer of the esophagus showed a statistically significant excess in the HBRA,

Table 1  
Estimates of relative risks for major cancer sites by dose-rate group (1979–1998)

Site of cancer	CA	RR (95% CI) for HBRA			
	RR	Low Group	Interm. Group	High Group	Subtotal
All cancers	1.00	1.08 (0.93–1.26)	1.00 (0.86–1.17)	0.92 (0.78–1.08)	1.00 (0.89–1.14)
Leukaemia	1.00	0.82 (0.35–1.86)	1.20 (0.57–2.56)	1.07 (0.47–2.39)	1.03 (0.56–2.02)
Solid cancers	1.00	1.10 (0.94–1.28)	0.99 (0.85–1.16)	0.91 (0.77–1.08)	1.00 (0.88–1.14)
Liver	1.00	1.07 (0.80–1.42)	0.84 (0.62–1.14)	0.74 (0.53–1.02)	0.89 (0.70–1.13)
Nasopharynx	1.00	0.96 (0.66–1.37)	0.98 (0.68–1.40)	0.88 (0.60–1.28)	0.94 (0.71–1.26)
Lung	1.00	0.93 (0.57–1.50)	0.67 (0.39–1.12)	1.04 (0.64–1.68)	0.87 (0.60–1.30)
Stomach	1.00	0.91 (0.55–1.48)	0.98 (0.60–1.57)	0.79 (0.46–1.33)	0.90 (0.61–1.34)
Esophagus	1.00	2.55 (0.91–8.21)	3.30 (1.26–10.24)	1.88 (0.60–6.37)	2.61(1.11–7.66)

Table 2  
Relative risks of non-cancer deaths excluding external causes

Factors		Control		HBRA	
		Cases	RR	Cases	RR (95% CI)
All		2847	1.00	7191	1.06 (1.01–1.10)*
Period	1979–1986	1233	1.00	3094	1.02 (0.95–1.09)
	1987–1998	1614	1.00	4097	1.09 (1.02–1.15)*
Sex	Female	1347	1.00	3353	1.05 (0.98–1.11)
	Male	1500	1.00	3838	1.06 (1.03–1.13)*
Age	0–39	285	1.00	992	1.31 (1.15–1.50)*
	40–49	90	1.00	305	1.28 (1.01–1.62)*
	50–59	208	1.00	525	1.00 (0.85–1.17)
	60–69	551	1.00	1288	1.06 (0.95–1.17)
	70+	1713	1.00	4081	1.01 (0.95–1.07)

\*  $P < 0.05$ .

RR=2.61 (95% CI, 1.11 to 7.66), and the trend test for the dose-rate group was not statistically significant ( $P=0.063$ ). The others showed no statistically significant difference between the HBRA and the CA. Among different dose-rate groups, the RRs did not show any monotonic trend, and slightly decreased cancer mortality was observed in the highest dose-rate group.

The ERR per Sv for all solid cancers associated with cumulative lifetime dose, which was the sum of external and internal radiation doses, was estimated to be  $-0.06$  (95% CI,  $-0.60$  to  $0.67$ ) for the entire HBRA and the CA.

### 3.2. Non-cancer mortality

The RR for non-cancer diseases excluding external cause mortality in the HBRA was 1.06 (95% CI, 1.01 to 1.10), and was significantly higher than that in the CA, but the excess was limited to those aged under 50 and in the latter half of the observation period (1987–1998) as shown in Table 2. In cause-specific analysis, a statistically significant increase in the HBRA was observed in viral hepatitis (RR=4.79; 95% CI, 1.73 to 19.83;  $P=0.001$ ) and chronic liver diseases (RR=1.50; 95% CI, 1.17 to 1.95;  $P=0.001$ ). On the other hand, the mortality of tuberculosis, the most common chronic infection in the study area, was lower in the HBRA than in the CA (RR=0.63; 95% CI, 0.54 to 0.74;  $P \leq 0.001$ ).

## 4. Discussion and conclusion

The current study provided a similar result to a previously reported one that the mortality for all cancers showed no significant difference between the HBRA and the CA; relative risk was estimated to be 1.00 (95% CI, 0.89 to 1.14). In site-specific analysis, an excess of esophageal cancer deaths was found in the HBRA. However, the RR for esophageal cancer did not show any increase in relation to the increase in radiation dose. This increase is difficult to explain by radiation exposure in view of recent risk estimates obtained from a study of A-bomb survivors [4], so further study is therefore necessary.

The accuracy of diagnosis is another concern in the present study. In this study, 26% of cancer deaths were from liver cancer, which is well known for its difficulty in diagnosis.

On the other hand, for cancer of the nasopharynx, which is the second most common cancer in the studied area (18%), the false-positive and false-negative rates can be assumed to be low because the evident clinical signs of nasopharyngeal cancer make its differential diagnosis relatively easy. On top of that, most types of cancer in the study area is fatal because cancer treatment is prohibitively expensive for most of the farmers in the area. This background information suggests that the numbers of false-positive and false-negative cases in ascertaining all-cancer deaths were small in the present study. It should also be noted that the sensitivity and specificity of ascertaining cancer deaths in the present study are unlikely to show any differences between the HBRA and the CA. The overall conclusion regarding the problem of the accuracy of diagnosis in present study is that our RR estimates may be biased toward the null value due to relatively low accuracy of diagnosis, but the magnitude of such biases is unlikely to be large. In fact, the RR of all cancers based on the diagnoses of pathology or hematology was not much different from that on the basis of all kinds of diagnoses: 0.99 (95% CI, 0.78 to 1.26) vs. 1.00 (95% CI, 0.89 to 1.14).

Another concern of significance here was the excess of non-cancer mortality in the HBRA, which is limited to those aged 50 years and younger, but it did not show a monotonic increase of mortality according to external radiation dose or cumulative lifetime dose. As we know, the follow-up study of atomic bomb survivors showed an excess of non-cancer deaths (ERR per Sv=0.14, 90% CI, 0.09 to 0.19), but the excess is much smaller than cancer risk [4]. On top of that, RR comparing the HBRA and the CA is expected to increase with age because lifetime radiation dose from natural sources is expected to increase with age. Taken together, these findings suggest that the statistically significant excess of non-cancer mortality does not seem to be attributable to natural radiation exposure but may be due to recent changes in lifestyle among those aged less than 50 years.

In conclusion, the present study showed no statistically significant increase of the mortality due to overall cancer in the HBRA; no radiation-related excess of site-specific cancer in the HBRA was found. The excess of esophageal cancer in the HBRA was not likely associated with exposure to high natural radiation. The observed increase of non-cancer mortality in the HBRA is unlikely to be attributable to radiation exposure; it may be due to recent changes in lifestyle of younger generations.

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